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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/801,471	03/15/2004	Joseph P. Lyssikatos	PC11078C	1808
23913	7590	11/10/2005	EXAMINER	
PFIZER INC 150 EAST 42ND STREET 5TH FLOOR - STOP 49 NEW YORK, NY 10017-5612			HOFFMAN, LEXINGTON A	
			ART UNIT	PAPER NUMBER
			1625	

DATE MAILED: 11/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/801,471	Applicant(s) LYSSIKATOS ET AL.	
	Examiner Lexington A. Hoffman	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29-35 is/are pending in the application.
- 4a) Of the above claim(s) 29-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 33-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>3/15/04</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Priority

This application is a divisional of 10/441567 (issued as US Patent 6734308), which is a divisional of 10/021201 (issued as US Patent 6645982), which claims benefit of 60/256598, filed 12/19/00.

Election/Restrictions

In response to the election/restriction requirement, applicant traversed the office's restriction and proposed an alternative grouping; namely grouping "process" claims (29-32), and "method" claims (33-35). If the office chose to prosecute the "method" claims, applicant would accept this restriction without traverse. Applicant's alternative grouping is recognized and claims 33-35 are examined in this office action. Claims 29-32 are withdrawn from consideration as being drawn to non-elected subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

a. *nature of the invention*

The instant invention is drawn to quinoline-based farnesyl transferase inhibitors, and their use in the treatment of disease.

b. state of the prior art and level of skill in the art

Farnesyl transferase inhibitors (FTIs) have been described as Kelland as a potential treatment for breast cancer, but with limited success for single-agent activity. Kelland feels FTIs will be more useful in combination therapy (Kelland, "Farnesyl transferase inhibitors in the treatment of breast cancer", *Expert Opin. Investig. Drugs* (2003), 12(3): 413-421 (statements from abstract)). Head, et al., share the view that FTIs may be most useful in combination therapy (Head, et al., "Protein farnesyltransferase inhibitors", *Expert Opin. Emerging Drugs*, 2003, 8(1): 163-178 (statement from abstract)). These authors further state "...it would appear that FTIs are unlikely to be used as monotherapy for advanced disease." (p. 174).

The level of skill in the FTI art is high.

c. predictability/unpredictability of the art

The high degree of unpredictability is well recognized in the FTI art. A slight change in the structure of a compound can significantly change its biological activity, as evidenced by the wide range of K-Ras FTase IC₅₀ (nM) values for structurally similar compounds described by Saha, et al., "Novel triazole based inhibitors of Ras farnesyl transferase", *Bioorganic and Medicinal Chemistry Letters* (2005), article in press, table 1 on p.2 of attached copy. When one combines an FTI with other pharmaceuticals that have different mechanisms of action and physiologic targets (as in claim 35), the results become even more unpredictable to due to possible synergism, antagonism, or toxic

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effects resulting from the combination. No data is provided on the results of combining the instant invention with any of the other listed pharmaceuticals.

d. *amount of guidance/working examples*

how to make

Preparation of example compounds is described. Its patentability is not further commented on as it is non-elected subject matter.

how to use

An *in vitro* procedure to assess inhibition of FT is described on p. 13 of the specification, but there is no indication that such a study was performed for the inventive compounds. No data is given for any *in vitro* or *in vivo* studies to give any indication of the pharmacologic effectiveness of the instant invention.

e. *breadth of the claims*

Applicant's assertion that the instant invention is effective in treating "hyperproliferative disorder" (claim 33), which would encompass all such disorders, whether benign or malignant, Ras-mediated or not, and the list of cancers in claim 34 is not commensurate with the objective enablement (the office acknowledges that applicant elected "lung cancer" in response to the election/restriction requirement, but in the interest of compact prosecution, the claims have been examined as written and hence include lung cancer). No data is given to link FTI with the treatment of thyroid, squamous cell, bladder, gastric (a few examples from claim 34), and Saha, et al. (previous citation) write that mutations in the K-ras isoform are most relevant to pancreatic, colon, and lung cancers (1st page). Additionally, the specification

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encompasses inhibition of Ras farnesyl transferase generically, and does not describe if the inventive compounds have different effects on the different isoforms (3 are described in Saha, et al.), nor the relationship between isoforms and specific cancers.

f. quantity of undue experimentation

Since insufficient teaching and guidance have been provided, one of ordinary skill in the art would be unable to use the inventive compounds without undue experimentation.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 34 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim embraces, among others, "head", "neck", and "gynecological" cancers. These terms are indefinite in the context of cancers. "Head" and "neck" are anatomic regions that contain bone, muscle, connective tissue, nervous tissue, lymph nodes, etc. Since cancers can originate from all these (and other) tissue types, it is not clear whether applicant intends the invention to be used on all cancers found in these regions, or cancers of only a certain type. It is confusing because "brain", "oesophageal", and "thyroid" cancers are claimed as well, and these cancers are found in the head and neck. Similarly, "gynecological" is indefinite, as this would technically include any cancer in a woman, including uterine, ovarian, and breast (the latter two are claimed in addition to "gynecological").

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Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lexington A. Hoffman whose telephone number is 571-272-4328. The examiner can normally be reached on Monday-Friday 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecelia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lexington Hoffman
Art Unit 1625

10/28/05 LH


Cecilia Tsang
Supervisory Patent Examiner
Art Unit 1625